a3 cancld- 31. The expression cassette according to claim 26 wherein said pathogenic agent is a tumor.

a4 34. A gene delivery vector comprising an expression cassette according to claim 26.

a5 44. A cell which contains a gene delivery vector according to claim 34.

REMARKS

Clams 1-25, 27, 32 and 45 are directed to non-elected subject matter and have therefore been cancelled.

Claim 26 has been amended to better describe the claimed invention. Claims 28, 30-31, 34 and 44 have been amended to correct dependencies. Claim 32 has been canceled because the pol II promoter claimed therein has been incorporated into independent claim 26.

Before continuing with the present Response to the Examiner's March 7, 2001 Office Action, the Applicants believe that a brief review of the claimed invention will render the following arguments more immediately understandable and alleviate the need for the Examiner to refer to the specification. The Applicants have invented and disclosed in their present application, gene delivery vectors that provide a means for enhanced immune responses against a wide range of pathogenic agents including, but not limited to, viruses, bacteria, parasites, fungi and tumors. The gene delivery vectors of the present invention are generally composed of nucleic acids contained within an appropriate gene delivery vehicle. The nucleic acids express both RNA transcripts that form double-stranded RNA (dsRNA) and also an antigen from a desired pathogenic agent. The dsRNA typically leads to the induction of various elements of the innate immune system including interferon production, while the antigen leads to induction of the adaptive immune response.

The following example is intended solely for descriptive purposes and not as a limitation or representative preferred embodiment. Rather, it is intended to highlight a few of the present invention's distinguishing characteristics. In one non-limiting embodiment, the gene delivery vector is plasmid DNA having a first nucleic acid molecule operably linked with a RNA polymerase III promoter that drives the expression

of non-protein expressing RNA that forms dsRNA. The plasmid DNA further includes an RNA polymerase II promoter operably linked to a second nucleic acid molecule that encodes for a tumor-associated antigen. As a result, a cell transformed using the gene delivery vector described above produces dsRNA and a recombinant tumor antigen. The dsRNA induces interferon production.

CLAIM OBJECTIONS

The Examiner has objected to claim 34 based on informality. Specifically, the Examiner has objected to the spelling of "anyone" in claim 34. Claim 34 has been amended to delete the term "anyone."

35 U.S.C. §112, SECOND PARAGRAPH REJECTIONS

The Examiner has rejected claims 31 and 32 under 35 U.S.C. §112 second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicants regard as the invention. Specifically, the Examiner states that claim 31 is drawn to a pathogenic agent that is a tumor. The Examiner asserts that tumors are not pathogenic agents. However, the Examiner is respectfully reminded that that the Applicants are permitted to use his or her own terminology, as long as it can be understood (see Manual of Patent Examining Procedure [M.P.E.P.] section 608.01(g)). Therefore, consistent with the cited provision of the M.P.E.P., the Applicants have elected to use of the term "pathogenic agent" as defined on page 12, lines 25-27 of the present application, to include tumors. Therefore, the Applicants respectfully assert that no claim amendment is required and the Examiners 35 U.S.C. §112 second paragraph rejection as to claim 31 has been traversed.

The Examiner has rejected claims 31 and 32 under 35 U.S.C. §112 first paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicants regard as the invention. Specifically, the Examiner states that claim 32 is drawn to an additional pol II promoter. Claim 32 has been canceled; therefore the Examiner's 35 U.S.C. §112 second paragraph rejection as to claim 32 is now moot.

35 U.S.C. §102(A) REJECTIONS

The Examiner has rejected claims 26, 28, 29, 32-35, 41, 43 and 44 as clearly anticipated by Polo, J.M and T.W. Dubensky, Jr. 1998. DNA vaccines with a kick. Nature Biotechnology 16: 517-518 (hereinafter Polo). Polo discloses DNA based alphavirus replicons expressing at least one gene of interest. Moreover, Polo suggests that co-expression of a cytokine from a gene delivery vehicle, together with a gene encoding for an antigen would provide improved vaccines. However, Polo does not disclose nor suggest a DNA cassette that expresses both double stranded RNA capable of inducing the production of interferon and an antigen from a pathogenic agent. Furthermore, claim 26 has been amended to recite an RNA polymerase II promoter operably linked to the nucleic acid molecule that encodes for an antigen. In the Polo article, the RNA polymerase II promoter simply directs the transcription of an alphavirus replicon RNA, whereas the gene of interest expressing the antigen is located within the alphavirus subgenomic region and its expression is completely under the direction of an alphavirus RNA dependent, RNA polymerase, NOT a DNA based promoter, as in the case of the present invention.

"Anticipation is established only when a single prior art reference discloses expressly or under the principles of inherency, each and every element of the claimed invention." RCA Corp. v. Applied Digital Data Systems, Inc., (1984, CA FC) 221 U.S.P.Q. 385. The standard for lack of novelty, that is, for "anticipation," is one of strict identity. To anticipate a claim, a patent or a single prior art reference must contain all of the essential elements of the particular claims. Schroeder v. Owens-Corning Fiberglass Corp., 514 F.2d 901, 185 U.S.P.Q. 723 (9th Cir. 1975); and Cool-Fin Elecs. Corp. v. International Elec. Research Corp., 491 F.2d 660, 180 U.S.P.Q. 481 (9th Cir. 1974). In the present Office Action, the Examiner's rejection is based on the Polo reference, which fails to show all of the essential elements of the instant invention.

Thus, while the Polo reference may teach similar data, the reference does not disclose an expression cassette having a promoter operably linked to a nucleic acid molecule which, when transcribed in vivo forms double-stranded RNA that induces the production of interferon and a RNA pol II promoter operably linked to a nucleic acid molecule that encodes an antigen. Therefore, the Applicants respectfully assert that the

Examiner's 35 U.S.C. §102 (a) rejections has been traversed and that claims 26, 28, 29, 32-35, 41, 43 and 44 are allowable over the cited reference.

35 U.S.C. §103(A) REJECTIONS

The Examiner has rejected claims 30, 31, 36-40 and 42 under 35 U.S.C. §103(a) as being unpatentable over Polo as applied to claims 26, 28, 29, 32-35, 41, 43 and 44 above, and further in view of Dubensky et al. in U.S. Patent 6,015,686 (hereinafter "Dubensky"). As presently amended, all pending claims depend from claim 26 which recites an expression cassette having a promoter operably linked to a nucleic acid molecule which, when transcribed in vivo forms double stranded RNA that induces the production of interferon and a RNA pol II promoter operably linked to a nucleic acid molecule that encodes an antigen.

The Examiner states that the claims are drawn to "an expression cassette expressing a tumor antigen and or/a pathogenic agent from a bacteria, parasite, or fungus in a delivery vehicle such as a retrovirus, herpesvirus, poxvirus, adenovirus, parvovirus and polyomavirus" (see the March 7, 2001 Office action, paper number 9 at page 3, third paragraph). The Examiner is reminded that a dependent claim is deemed to include all of the limitations found in the claim from which it depends (see 35 U.S.C. §112 fourth paragraph). Therefore, the Applicants respectfully assert that the claims presently rejected include the elements as presently stated in claim 26, the independent claim. As previously discussed above, Polo does not disclose or even remotely suggest, a DNA cassette that expresses RNA that forms double stranded RNA capable of inducing the production of interferon and a RNA pol II promoter operably linked to the nucleic acid molecule that encodes for an antigen.

Moreover, the Dubensky reference discloses alphavirus based ELVS vectors that are also composed generally of DNA-based promoters (or their equivalent) that direct the transcription of the alphavirus replicon RNA, wherein a gene of interest expressing antigen(s) is located within the alphavirus subgenomic region under the control of an alphavirus RNA dependent, RNA polymerase. In fact, the Polo reference and the Dubensky reference teach essentially the same general concepts (note that Polo and Dubensky are co-authors on the Polo references, inventors on the Dubensky reference and also inventors on the present application).

Persons having ordinary skill in the art would not be motivated to produce the novel expression cassettes of the present invention using the teachings of the Polo and Dubensky references. Polo and Dubensky both teach an alphavirus vector construct having a DNA dependent, RNA polymerase (e.g., pol II) promoter that directs the transcription of the replicon RNA whereas the gene of interest expressing the pathogen derived antigen is located in the alphavirus sub-genomic region and is under the direction of an alphavirus RNA dependent, RNA polymerase. The present invention teaches a plasmid having at least two discrete nucleic acid sequences. One nucleic acid sequence encodes for double stranded RNA that induces interferon production AND at least one other nucleic acid sequence encodes for a pathogen derived antigen. The nucleic acid sequence that encodes for the pathogen derived antigen of the present application is under the direction of a DNA dependent, RNA polymerase II promoter, NOT an RNA dependent, RNA polymerase promoter as is the case of the cited alphavirus prior art. It is well known in the art that these are very different categories of promoters. Therefore, it would not be logical to combine these references for the purposes stated by the Examiner, nor would there be any reasonable expectation of success. Consequently, absent a clear and particular motivation to combine these particular references and a reasonable expectation of success, there can be no 35 U.S.C. §103 (a) rejection based on these references. Simply put, the cited references are not related to the present invention. Both are deficient in many of the technical concepts and teachings needed to practice the present invention and the combination of these two references cannot, and do not, make up these deficiencies. Persons of ordinary skill in the art would not look to the cited references, either individually or in combination to practice the invention as presently claimed.

Therefore, the Applicants respectfully assert that the Examiner's 35 U.S.C. §103(a) rejection has been traversed and the claims 30, 31, 36-40, and 42 are allowable over the cited references.

CONCLUSION

If it is felt for any reason that direct communication with Applicants' attorney would serve to advance prosecution of this case to finality, the Examiner is invited to call the undersigned attorney at the below listed telephone number.

Appendix A is attached for the Examiner's convenience showing the entire claim set as pending (post amendment) in the present application.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 16-2230.

Respectfully submitted,

August 10, 2001

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Version With Markings To Show Changes Mad

26 An expression cassette comprising a [first] promoter operably linked to a nucleic acid molecule which, when transcribed in vivo forms a double stranded RNA that induces the production of interferon, and an [second] RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

28. The expression cassette according to claim 26 [or 27] wherein said antigen is a viral antigen.

30. The expression cassette according to claim 26 [or 27] wherein said pathogenic agent is a bacteria, parasite or fungus.

31. The expression cassette according to claim 26 [or 27] wherein said pathogenic agent is a tumor.

34. A gene deliver vector comprising an expression cassette according to [anyone of claims 1, 5, 9 or 27] claim 26.

44. A cell which contains [an expression cassette according to claim 1 or] a gene delivery vector according to claim 34.

APPENDIX A
CLAIMS AS PRESENTLY PENDING
09/546,201

26. An expression cassette, comprising a promoter operably linked to a nucleic acid molecule which, when transcribed *in vivo*, forms double stranded RNA that induces the production of interferon, and an RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

28. The expression cassette according to claim 26 wherein said antigen is a viral antigen.

29. The expression cassette according to claim 28 wherein said viral antigen is from a virus selected from the group consisting of HIV, HSV, HBV, HCV, HPV, and FIV.

30. The expression cassette according to claim 26 wherein said pathogenic agent is a bacteria, parasite or fungus.

31. The expression cassette according to claim 26 wherein said pathogenic agent is a tumor.

33. The expression cassette according to claim 26 wherein said pol II promoter is selected from the group consisting of CMV, SV40, MoMLV LTR and RSV LTR.

34. A gene delivery vector, comprising an expression cassette according to claim 26.

35. The gene delivery vector according to claim 34 wherein said vector is a plasmid.

36. The gene delivery vector according to claim 34 wherein said vector is a recombinant retrovirus.

37. The gene delivery vector according to claim 34 wherein said vector is a recombinant herpesvirus.

38. The gene delivery vector according to claim 34 wherein said vector is a recombinant poxvirus.

39. The gene delivery vector according to claim 34 wherein said vector is a recombinant adenovirus.

40. The gene delivery vector according to claim 34 wherein said vector is a recombinant parvovirus.

41. The gene delivery vector according to claim 34 wherein said vector is a recombinant alphavirus.

42. The gene delivery vector according to claim 34 wherein said vector is a recombinant polyoma virus.

43. The gene delivery vector according to claim 34 wherein said vector is a eukaryotic layered vector initiation system.

44. A cell which contains a gene delivery vector according to claim 34.